

his commercial instincts, his scientific or technical skill and pride. He will be well educated as to knowledge and methods. He will have the wisdom to use this knowledge in practice with a due sense of proportion of the value in the recognition of disease, of history, observation, and instrumental and laboratory examinations. He will not pretend to know all or to do all as rightly could our practitioners of fifty or seventy-five years ago. He himself will do much less than they did. He will recognize his own limitations and appeal oftener to the expert. Between him and the expert there will be the cordial relation of colleagues and not the antagonism of rivals for trade-gain or reputation. He will be no second-rate product of our medical schools, but one of first rank. He will be practical, but inspired to ever improving work by the spirit of investigation. While clinging fast to that which is good of the old he will be no slave to tradition, but will be able to throw aside the disproved old for the proved new. He will be, and will be regarded as being, a scientific man. He will become the family confidant as of yore, the family adviser, well recompensed for his services. He will be self-respecting and respected by others.

122 South Michigan Avenue.

#### OBSERVATIONS ON BLOOD SEDIMENTATION IN TUBERCULOUS PATIENTS\*

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IN an article on "Blood Sedimentation Test as an Aid in Diagnosis in Surgical Infections," Friedlander<sup>1</sup> supplies the following definition: "The sedimentation time of the human red blood corpuscles is a non-specific biological reaction indicating the suspension stability of the erythrocytes in blood which has been rendered non-coagulable. The sedimentation test consists in observing the varying speed with which the erythrocytes, in a specially constructed tube, are separated from the plasma"; and, he adds, "It is of great importance to note whether there can be established a definite correlation between pathologic conditions and the length of time required for the sedimentation of the red corpuscles."

#### EARLY BLOOD SEDIMENTATION INVESTIGATIONS

So much has been written on the subject since 1918, when Fahraeus<sup>2</sup> discovered the decreased suspension stability of red blood corpuscles during pregnancy, that it is unnecessary to go into the history of the sedimentation phenomenon other than to state that for centuries it has been known that in certain diseases, characterized by inflammation and fever, the erythrocytes sedimented more quickly than was usual in the case of blood drawn from healthy individuals. In fact it was recognized during that period of medical therapeutics when bleeding was a common therapeutic measure, that rapid settling

of the blood cells was a symptom of grave significance. Following this discovery of Fahraeus many clinicians and laboratory workers investigated the blood sedimentation rate as an aid in diagnosis and prognosis in many varied surgical and medical conditions. A recent study by Cutler<sup>3</sup> of Philadelphia on blood sedimentation in tuberculosis was the stimulus for the present work. The reports of Cutler and others<sup>4,5</sup> indicate that by observing the rate of sedimentation of the red blood corpuscles, one has at his command a very valuable aid for determining the amount of activity present in tuberculous foci and that such information, especially when supplemented by repeated tests in the same individual, can supply a very important aid in reaching a decision as to prognosis.

Heretofore tuberculosis workers have labored under a tremendous handicap by having at their command no reliable tests upon which to base a definite opinion as to the amount and character of activity in tuberculous foci nor as to the individual patient's ability to exercise or resume work. It is true that the physician of experience in treating tuberculous patients can, as a result of observation and study of many patients, reach a point where his judgment in such matters attains a considerable degree of skill. His judgment is based upon the presence or absence of temperature, the character and rate of the pulse, the character and amount of cough and expectoration and the presence or absence of hemoptysis, pleurisy and digestive disturbances, by blood pressure readings, by physical and x-ray examinations and by observation and evaluation of a score of different signs and symptoms. But in spite of the greatest of experience and the best of judgment, errors will arise. Patients with doubtful prognoses will return to work and progress favorably, while others with apparently good prognoses will relapse. If then to this experience and judgment derived from observation and study can be added the simple test of blood sedimentation with the result that the percentage of error can be further reduced, a great step forward will be accomplished.

#### BLOOD SEDIMENTATION TESTS IN TUBERCULOSIS

Explained briefly the value of the test depends upon the following facts and premises:

1. When human blood is mixed with sodium citrate solution, so as to render it non-coagulable, and is placed in graduated test tubes and allowed to stand at room temperature, the red blood cells slowly settle toward the bottom of the tube leaving a supernatant layer of clear serum.

2. In normal healthy individuals this settling takes place very slowly. In women the settling may be slightly more rapid than in men and more rapid in menstruating than in non-menstruating women. These differences are not, however, great enough to affect the value of the test.

3. In cases of arrested tuberculosis the settling of the erythrocytes is not markedly different from that seen in normal blood.

4. In quiescent tuberculosis the rate of settling is slightly more rapid and more pronounced.

5. In active and very active tuberculosis the rate is much accelerated, the rate of settling being apparently, in a majority of cases, closely related to

\* Read before the Regional Meeting of the American College of Surgeons, Sacramento, April 7, 1927.

the amount of activity and the seriousness of the disease.

#### CLASSIFICATION OF THE PATIENTS TESTED

In an attempt to correlate the sedimentation rate and the degree of activity, it was necessary to determine in advance the proper classification of the individual patients used in this experiment. This, it seemed to us, was the most important part of the problem or at least the part most fraught with error. It was decided that one of us (O'Connor) should have complete charge of collecting the blood specimens and make the sedimentation readings, while the other two (Peers, Durand), having the patients under daily observation, should make the classifications. The list of patients' names was supplied to us by the technician, and were classified by us into the following groups:

1. Apparently arrested, including working and non-working cases.
2. Quiescent.
3. Mildly active to quiescent; condition doubtful.
4. Mildly to moderately active.
5. Very active.

This classification was based:

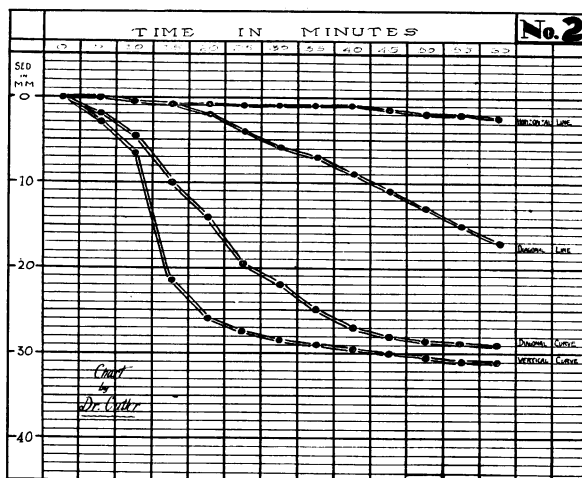
(a) In apparently arrested and quiescent cases, upon the length of time they had been free from fever and other signs of toxemia and upon the amount of exercise they could take or the work they could perform without signs of reaction.

(b) In active or very active, upon the severity and the number of the symptoms of toxemia and the length of time such symptoms and such severity had existed. The improvement or non-improvement or increase of symptoms was also taken into consideration.

The presence or absence of cough or expectoration or the presence or absence of bacilli in the sputum was not considered in the classification except that the occurrence of increased cough and expectoration was considered as evidence of activity even where other signs were absent. The classification was made as nearly correct as possible upon the experience and judgment gained by daily contact over a period of years in the treatment of many thousand patients and without attempting to make

individual patients fall into a class governed by strict fast rules.

Each of us (Peers, Durand) had a separate list of patients and classified each patient without consulting the other. When lists were compared it was



found that the classification agreed with a very small margin of difference.

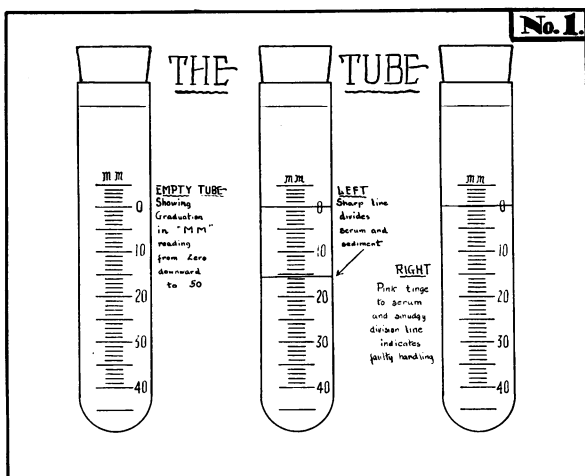
#### TECHNIQUE OF SEDIMENTATION TEST

The technique of Cutler, as described in the above-mentioned article, was used throughout, as were also the tube and sedimentation charts described by him. The type of tube is shown in Fig. 1. It is of 10 cc. capacity and graduated up to 5 cc.'s in tenths of a cubic centimeter and marked in millimeters. It is necessary that needles, syringe, and tubes be clean and dry.

A 5 cc. syringe with 20 gauge needle was used. Into this was drawn  $\frac{3}{4}$  cc. of freshly prepared 3 per cent sodium citrate solution. The inside of the syringe was moistened throughout with the citrate solution and then enough of it expelled to leave exactly  $\frac{1}{2}$  cc. in the syringe. The cubital vein was punctured and  $4\frac{1}{2}$  cc. of blood added to the citrate solution. The needle was then withdrawn and removed. The barrel of the syringe was then drawn back and the contents mixed by carefully tilting the syringe back and forth until the solution and the blood were thoroughly mixed. The blood was then transferred to the sedimentation tube.

The blood was collected between 9 and 11 a. m., and the readings made within four or five hours. Usually five or six tubes were taken in the morning and allowed to stand in a rack with the tubes stoppered with paraffin-coated corks. Before reading, the rack and tubes were gently inverted several times so as to obtain a uniform suspension of the blood cells in the citrated plasma.

The readings were recorded on Doctor Cutler's sedimentation charts on which the horizontal lines represent the divisions in the sedimentation tubes and the vertical lines represent the interval of time, each vertical line representing five minutes of elapsed time (Chart 2). By recording on the chart each five minutes the millimeter reading on the blood tube, a graph is made from which the velocity of sedimentation at any period is easily noted. The sedimentation chart is a very ingenious and excellent



tation was considered as evidence of activity even where other signs were absent. The classification was made as nearly correct as possible upon the experience and judgment gained by daily contact over a period of years in the treatment of many thousand patients and without attempting to make

method of illustrating in a graphic manner just what happens in each particular blood studied. It makes a permanent record and is particularly valuable because a series of blood tests from the same patient can be recorded on one chart, thus furnishing an easy and quick method of estimating the correlation, if any, between changes in the clinical course of the patient's disease and changes in the manner of blood sedimentation.

#### INTERPRETATION OF SEDIMENTATION TEST

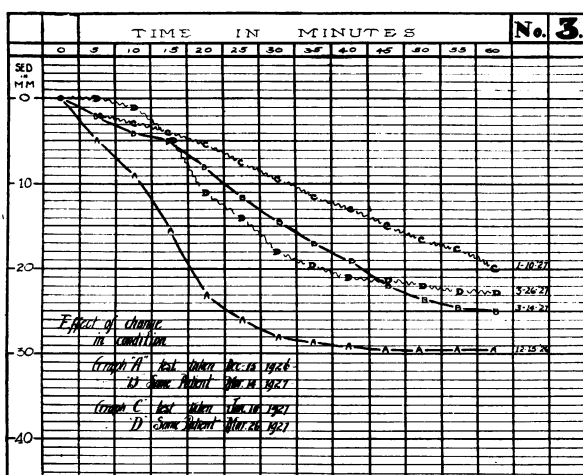
If there is a definite relation between the degree of tuberculous activity and the sedimentation stability of the blood and if, with disease activity, the blood sediments more rapidly according to the degree of activity, this should be clearly shown on the chart. This will be shown in two ways:

First, by the sedimentation time which is the number of minutes from the commencement of the count until the cells are beginning to pack and the sedimentation has definitely slowed up, which, in normal individuals, is always a period of several hours.

Second, by the sedimentation index which is defined by Cutler as "the total sedimentation of red blood cells at the end of sixty minutes expressed in millimeters."

In the normal person this sedimentation index should not fall below 10 mm. and may be as low as 2 or 4 mm.

The graphic chart should then, in normal humans, show an almost horizontal line when the sedimentation is charted. With departure from the normal, the index should be higher and the line assume a more diagonal course. In very active cases the line should, and does, drop more rapidly, and frequently shows a sedimentation time of between twenty and thirty minutes instead of several hours and a sedimentation index of between 10 and 30 mm. instead of a normal of less than 10 mm. with an average of 5 or less.

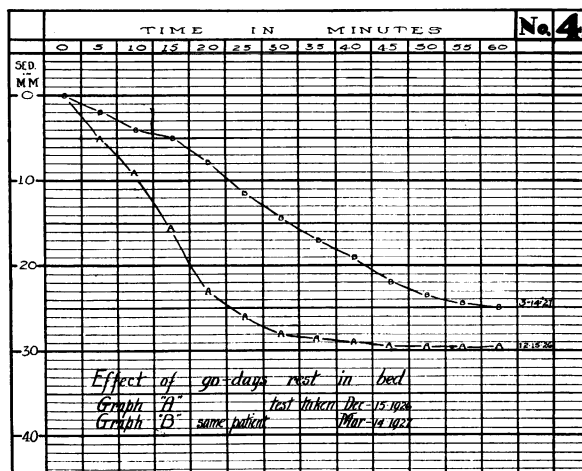


Cutler gives four graphs as the probable sedimentation lines to be seen in different types:

- A horizontal line as seen in normal persons or in arrested tuberculous patients.
- A diagonal line as seen in quiescence.

(c) A so-called "diagonal curve" representing slightly or moderately active disease.

(d) A so-called "vertical curve" representing moderately to markedly active cases. These are shown on Chart No. 2.



#### RESULTS IN 126 CASES STUDIED

Our series consisted of 126 cases classified as follows:

- Apparently arrested, sixteen cases.
- Quiescent, twenty-one cases.
- Doubtful quiescent, nine cases.
- Mildly or moderately active, fifty cases.
- Very active, thirty cases.

Our findings, in the main, agree with Cutler. Our apparently arrested cases, many of them working, some for many years, almost uniformly showed a horizontal line with a low sedimentation index. Our very active cases showed, almost always, a diagonal or a vertical curve, except that our percentage of vertical curves was not so great as we should have expected.

On the other hand quite a high percentage of our quiescent cases gave a horizontal line. Also some of our mildly active cases, from a clinical point of view, gave a diagonal or quiescent line. These differences are probably due to one or more of three things:

1. The fact that no series of sedimentation tests can be expected to run true to form to the extent of 100 per cent.

2. The average sedimentation index as shown by Doctor Cutler may be too high for quiescent and mildly active cases.

3. We may have been too conservative in our classification and have erred in placing our patients in a class more unfavorable than that to which they were entitled. In this respect, however, we noticed that three of our active cases which gave a quiescent, or nearly quiescent line, developed shortly thereafter quite acute exacerbations, thus confirming the clinical judgment rather than the blood sedimentation picture. In two of these three cases, however, the sedimentation at the end of two hours showed a very marked drop such as was not seen in the two-hour pictures of our arrested or definitely quiescent group; which may indicate that there may,

in some cases, be a delayed sedimentation and that perhaps more attention should be paid to the two-hour sedimentation index in suspected active cases.

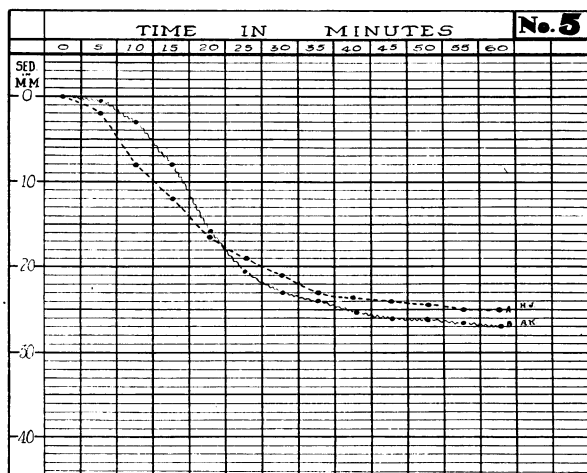
#### OTHER CHART INTERPRETATIONS

Chart No. 3 shows the curves on two patients where, in each, two different sedimentation tests were taken after a period of several weeks. The lines marked A and B represent the curves of one patient with an interval of three months—curve A being the result of a test taken on December 15, 1926; curve B being taken March 14, 1927. This patient, a very advanced case classified as very active, was put on bed rest and, no improvement being shown in her condition, was, after an interval of several weeks, given pneumothorax treatment with evident clinical improvement. Curve B showing a slower and less marked sedimentation would, in this case, seem to bear out the clinical evidence of lessened activity.

Lines C and D give the opposite picture. Line C shows the result of a test taken January 10, 1927, in the case of a patient with normal temperature, marked gain in weight and without any marked symptoms of toxemia. His sputum was negative for tubercle bacilli on numerous occasions. He was classified by us as active in spite of good general condition. His sedimentation curve, however, approached very closely the diagonal line of quiescence. March 20, he developed a typical exacerbation, and the line D shows the change to the diagonal curve of activity following a test taken March 26, 1927. It is of interest also to remark that his sputum was positive for the first time in nine months.

Chart No. 4 is another graph showing a separate picture of the improvement shown by lines A and B in Chart No. 3.

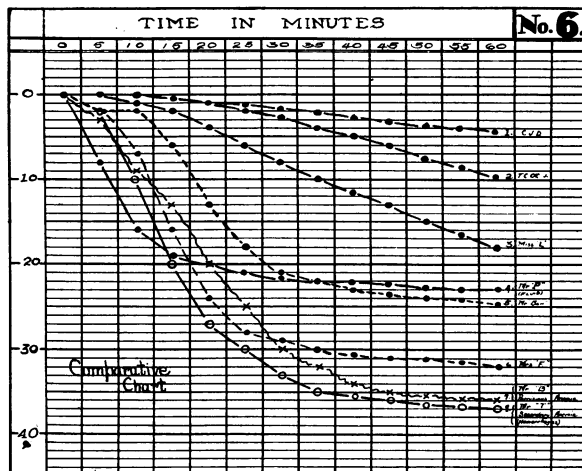
Chart No. 5 shows two interesting curves bearing out the judgment of the clinician based on his knowledge of the patients as a result of long observation. A is an advanced patient whose disease has been apparently quiescent for many months but who was classed as active and whose exercise has



been very closely supervised. Because, however, of the chronicity of his disease, he has been allowed to do a little clerical work at the institution to keep his mind occupied and to pay his expenses. He is allowed two or three hours per day keeping books.

He has, however, not been allowed to think of returning to work. His curve would seem to support the need of continuing his present mode of life.

Patient B is an advanced patient whose disease, as far as symptoms are concerned, has been appar-



ently quiescent for several months. His clinicians classed him as active and have limited his exercise to fifteen minutes per day, although other patients, with the same clinical history, are allowed as much as forty minutes. The curve B would seem to show the clinicians' judgment to be correct and would indicate that patient B requires careful supervision in spite of long and continued normal temperature, good weight and feeling of well-being.

Chart No. 6 gives a comparison of the graphs of different types of patients:

No. 1 is an apparently arrested case who has been working ten years.

No. 2 was classified by us as quiescent and yet falls within the extreme normal limit. This is a pneumothorax patient still under treatment but able to do some work.

No. 3 was classified by one of us as mildly active and by the other as quiescent. She has the quiescent or diagonal line.

No. 4 is a quite markedly active case, according to our classification—a case of hydropneumothorax. His curve shows a very quick drop, but the sedimentation index is only 23 mm.

No. 5 is a very advanced and, we consider, a very active case—more so than No. 4—but his drop is not so rapid although his one-hour index is slightly greater.

No. 6 is a very active advanced case with, we think, a hopeless prognosis. She has a quick drop and a high index.

No. 7 is one of pernicious anemia sent to us because of supposed tuberculosis which our examination failed to disclose. His curve is shown, as it bears out other authorities regarding the graph seen in pernicious anemia.

No. 8 is a case of advanced active pulmonary tuberculosis with tuberculosis complications and with a marked secondary anemia. He has the highest sedimentation index of all.

Chart No. 7 illustrates the appearance of the sedimented blood in the tubes as seen in six of the

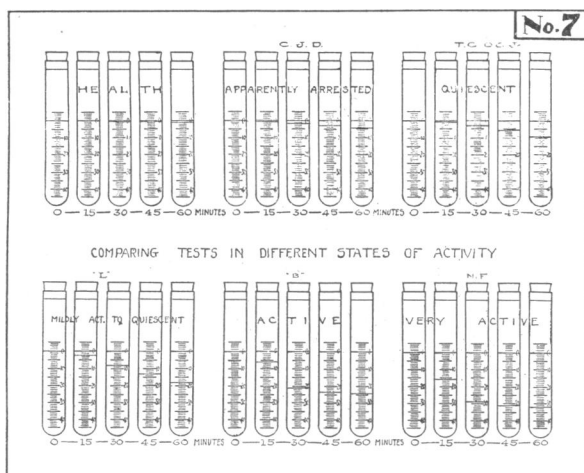
eight patients whose graphs were shown on Chart No. 6.

Chart No. 8 shows in percentage figures how the total number of patients on the different classifications were divided when classed according to the various lines of Cutler. This table seems to indicate to us that we have been perhaps too conservative in our classification and have placed a number of the apparently arrested cases in the quiescent group and have called mildly active many who were really quiescent. That is our feeling. Time alone will furnish the truth of the matter. After a year or two of follow-up we will be in a much better position to offer a definite opinion. The percentage table does, however, show one thing very strikingly and that is, that with the increase of activity there is a distinct shift to the right of the table. Thus, while at the top of the list the apparently arrested show 87.5 per cent of horizontal lines and 12.5 per cent of diagonal lines there are no diagonal or vertical curves, while at the lower end of the list in the case of the very active there are no horizontal lines, only 9.9 per cent of diagonal lines with 69.9 per cent of diagonal curves and 19.9 per cent of vertical curves. It is in the grades between, the quiescent cases and those from quiescent to moderately active, where the phenomenon of sedimentation is not so strikingly helpful. This may mean a large percentage of error in classification or it may mean that those patients in these middle classes whose graphs fall in the horizontal lines are, while more or less active, those with good prognoses; while those falling in the diagonal curve, even though apparently quiescent, are in the danger group. Time and follow-ups should help solve this problem.

#### CONCLUSIONS

From the study we have made we would draw the following conclusions:

1. That there is a very definite tendency to sedimentation instability of the erythrocytes in the blood of tuberculous patients.



2. That there is a more or less definite relation between the degree of tuberculous activity and the sedimentation index of the patient's blood.

3. That this relation is shown by the tendency of the sedimentation index to approach the normal as

patients improve and as their disease becomes quiescent or arrested.

4. That the sedimentation index in a majority of cases of active disease shows a sedimentation index away from the normal in proportion to the activity

TABLE OF PERCENTAGES <span style="float: right;">No. 8</span>				
CLINICAL CONDITION	HORIZONTAL LINE	DIAGONAL LINE	DIAGONAL CURVE	VERTICAL CURVE
APPARENTLY ARRESTED	87.5%	12.5%		
QUIESCENT	47.6%	38.1%	14.3%	
MILDLY ACTIVE TO QUIESCENT	44.4%	44.4%	11.2%	
MILDLY TO MODERATELY ACTIVE	24. %	26. %	50. %	
VERY ACTIVE		9.9%	69.9%	19.9 %

and to the seriousness of the patient's condition.

5. That the evidence furnished by the sedimentation index cannot at present be allowed to outweigh other evidence, but must be considered merely as additional data in summing up the estimation of activity or in determining the prognosis.

6. It may well be that one of the great benefits to be derived from this test will be from a study of a series of tests taken from time to time on each individual during the period of sanatorium residence. We feel that such serial tests will probably be of much greater value than single tests.

Colfax School for the Tuberculous.

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4. Waugh: *The Canadian Medical Association Journal*, 1923, p. 604.
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Dr. Abraham Zingher, noted bacteriologist who helped to perfect the Schick test for susceptibility to diphtheria, was asphyxiated June 5 in his laboratory in New York, while he dozed in his chair. He was conducting research into the Dick test for scarlet fever. The gas tube to a burner over which he was heating a test tube became disconnected while he slept. The body was found by Mrs. Zingher. The doctor was 42 years old. He had suffered a stroke of facial paralysis once before, and Doctor Gonzales, assistant medical examiner of the New York health department, who investigated the death, expressed the belief that he had suffered a second stroke while at his work. A sheaf of new-made notes lay beside him on the table on which his head rested when he was found.—*Ohio Health News*.